

95 Compressive strength 83.25 MPa  
Flexural Strength 64.31 MPa.--

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IN THE CLAIMS:

Please cancel claim 86.

In claim 87, please replace the as-filed claim with the following replacement claim:

96 -- 87(amended). A powder mixture for producing a bone cement comprising contrast agent grains having a D<sub>50</sub> grain size of at least 3 um.--

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REMARKS

Applicant respectfully requests entry of the above amendments, and early action upon the above-captioned patent application.

Applicants submit that the above change introduce no new matter. Support for the amendment to claim 87 is found at page 37, line 13 of the as-filed application.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The first page of the attachment is captioned "Version with markings to show changes made".

Please provide any extensions of time which may be necessary and charge any fees which may be due to Deposit Account No. 10-0750, but do not include any payment of issue fees.

Respectfully submitted,

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## VERSION WITH MARKINGS TO SHOW CHANGES MADE

### IN THE SPECIFICATION:

The paragraph beginning at page 27, line 30 has been amended as follows:

[In general, Table I reveals that, in the range of 20-40 wt% BaSO<sub>4</sub>, the cement had sufficient radio-opacity and was mechanically sound.] However, it was further observed that the shelf life of at least the 28 wt% embodiment of these above mixtures (represented as Run 1 below) was less than optimal for use in vertebroplasty. In particular, embodiments which were aged up to 6 months displayed significantly higher setting times than similar non-aged embodiments, thereby demonstrating that this embodiment possessed a short shelf-life. Accordingly, three additional formulations (Runs 2-4 below) of barium sulfate-containing bone cement were evaluated, and these approximate formulations are presented in Table II below:

The paragraph beginning at page 31, line 10 has been amended as follows:

In addition, review of TABLE IV indicates that the increased BaSO<sub>4</sub> concentrations in the mixtures of the present invention yield longer setting times (about 18-20 minutes) than those of cements having lower contrast agent fractions, such as the 16.67 wt% embodiment of Table I (about 17 1/4 minutes). [ For the purpose of the present invention, the setting time of a cement is determined by ISO 5833, carried out at an ambient temperature of 23 °C. ] Long setting times are attractive for vertebroplastic bone cements because, in use, the cement must be able to suitably flow from the injection gun through a small tube to the vertebral body, and then refrain from leaking from the vertebral body once it is in place. Accordingly, a vertebroplastic cement should avoid setting for at least 10 minutes, and more preferably for much longer time periods such as 14-20 minutes, with some embodiments being in the range of 18-20 minutes. Most conventional orthopaedic barium sulfate-containing bone cements typically have setting

times on the order of 8-12 minutes, and so are inadequate for this application. Combs reported setting times of no more than only 15 minutes, albeit at an ambient temperature of about 30 °C. Without wishing to be tied to a theory, it is believed that the reason for Jensen's selection of "slow setting" Cranioplastic as the base material for a vertebroplastic cement could have been this long setting time feature. However, TABLE I indicates that the 16.5-18.8 wt% mixtures described by Jensen probably had setting times of about 17 1/4 minutes.

The entire paragraph at page 37, lines 4-6 has been deleted.

The paragraph beginning at page 37, line 10 has been amended as follows:

Therefore, in accordance with the present invention, there is provided a powder mixture for producing bone cement, the mixture comprising contrast agent grains (preferably, barium sulfate grains) having a  $D_{50}$  grain size of at least  $[2\text{ }\mu\text{m}$ , preferably at least  $3\text{ }\mu\text{m}$ , more preferably at least  $5\text{ }\mu\text{m}$ , and most preferably at least  $10\text{ }\mu\text{m}$ . In some embodiments, the  $D_{50}$  grain size is between 6 and  $14\text{ }\mu\text{m}$ . These coarse grain embodiments provide particular advantage to high  $\text{BaSO}_4$ -containing powder mixtures, such as those powder mixtures comprising between 20 wt% and 40 wt%  $\text{BaSO}_4$  in that the coarse grains do not form strength-degrading agglomerates. Preferably, the  $\text{BaSO}_4$  grains are not embedded within the PMMA powder. In preferred embodiments of powder mixtures containing coarse, high wt%  $\text{BaSO}_4$  powder, more than 50 wt% of the BPO is unbound or "free" (preferably, at least 75 wt%). Free BPO is advantageous over bound BPO in that it can more quickly initiate the bone cement polymerization reaction, and so help adjust desired setting times.

The paragraph beginning at page 39, line 13 has been amended as follows:

Next, it was further found that replacing barium sulfate with zirconia grains in the powder mixture also produced a bone cement mixture having sufficient radio-opacity and

shelf life. In particular, one cement of the present invention containing about 20 wt% monoclinic zirconia was found to have the following mechanical properties:

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Flexural Strength 64.31 MPa

[Flexural Modulus 2454 GPa].

#### IN THE CLAIMS:

Claim 86 has been cancelled.

Claim 87 has been amended as follows:

87(amended). A powder mixture for producing a bone cement comprising contrast agent grains having a  $D_{50}$  grain size of at least [2] 3  $\mu\text{m}$ .